Effect of application of a PVP-iodine solution before and during subgingival ultrasonic instrumentation on post-treatment bacteremia: A randomized single-center placebo-controlled clinical trial

Sahrmann, P ; Manz, A ; Attin, T ; Zbinden, R ; Schmidlin, P R

Abstract: BACKGROUND: To assess the effect of concomitant subgingival rinsing with 10% PVP-iodine during subgingival instrumentation on the prevalence and magnitude of bacteremia of oral origin. MATERIALS AND METHODS: Subgingival instrumentation was performed with water or PVP-iodine rinse in patients with periodontitis. Prior to instrumentation, subjects gargled for 1 min with the allocated liquid. Pockets were then rinsed for 1 min and subgingivally instrumented with liquid-cooled (water/PVP-iodine) ultrasonic scalers (1 min). Two minutes later, a blood sample from the arm vein was drawn using a lysis centrifugation blood culture system for quantitative microbiological analysis. Non-parametric statistical tests were performed to assess differences in the prevalence and extent of bacteremia between groups. RESULTS: Of the 19 samples in each group, oral-borne bacteremia was detected in 10 of the control and 2 of the test samples. With an average of 3.0 [1;5] colony forming units, significantly less bacteria and bacteremia were found in the test group compared to the controls (12.2 [1;46]) (p=0.003). Anaerobic bacteria were not found in the test group. CONCLUSIONS: Bacteremia after subgingival instrumentation with concomitant PCP-iodine rinsing is reduced but not eliminated. Therefore, it might be recommended for patients at a high risk of endocarditis or infection of endoprostheses. However, preventive antibiotic treatment should not be omitted.

DOI: https://doi.org/10.1111/jcpe.12416

Originally published at:
Sahrmann, P; Manz, A; Attin, T; Zbinden, R; Schmidlin, P R (2015). Effect of application of a PVP-iodine solution before and during subgingival ultrasonic instrumentation on post-treatment bacteremia: A randomized single-center placebo-controlled clinical trial. Journal of Clinical Periodontology, 42(7):632-639.
DOI: https://doi.org/10.1111/jcpe.12416

Effect of application of a PVP-iodine solution before and during subgingival ultrasonic instrumentation on post-treatment bacteremia: A randomized single-center placebo-controlled clinical trial.

Sahrmann P[1], Manz A[1], Attin T[1], Zbinden R[2*], Schmidlin PR[1*]

[1] Clinic of Preventive Dentistry, Cariology and Periodontology, Center of Dental Medicine, University of Zurich, Switzerland

[2] Institute of Medical Microbiology, University of Zurich, Switzerland

* Both authors denoted with an asterisk contributed equally to this study and share last authorship

Corresponding author:
Philipp Sahrmann
Dr. med. dent., MAS in Periodontology (University of Zurich)
Clinic of Preventive Dentistry, Periodontology and Cariology
Center of Dental Medicine, University of Zurich
Plattenstrasse 11, CH-8032 Zurich, Switzerland
Phone: +41 44 634 34 12, Fax: +41 44 634 43 05
E-Mail: philipp.sahrmann@zzm.uzh.ch

Running title: PVP-iodine reduces bacteremia

Keywords: Antiseptics, periodontitis, bacteremia, ultrasonic debridement, RCT

Conflict of interest and sources of funding: The authors declare that there are no conflicts of interest regarding the present study. There was no external funding apart from the support of the Clinic of Preventive Dentistry, Periodontology and Cariology, University of Zurich.

Abstract

Background: To assess the effect of concomitant subgingival rinsing with 10% PVP-iodine during subgingival instrumentation on the prevalence and magnitude of bacteremia of oral origin.

Materials and Methods: Subgingival instrumentation was performed with water or PVP-iodine rinse in patients with periodontitis. Prior to instrumentation, subjects gargled for 1 min with the allocated liquid. Pockets were then rinsed for 1 min and subgingivally instrumented with liquid-cooled (water/PVP-iodine) ultrasonic scalers (1 min). Two minutes later, a blood sample from the arm vein was drawn using a lysis centrifugation blood culture system for quantitative microbiological analysis. Non-parametric statistical tests were performed to assess differences in the prevalence and extent of bacteremia between groups.

Results: Of the 19 samples in each group, oral-borne bacteremia was detected in 10 of the control and 2 of the test samples. With an average of 3.0 [1;5] colony forming units, significantly less bacteria and bacteremia were found in the test group compared to the controls (12.2 [1;46]) (p=0.003). Anaerobic bacteria were not found in the test group.

Conclusions: Bacteremia after subgingival instrumentation with concomitant PCP-iodine rinsing is reduced but not eliminated. Therefore, it might be recommended for patients at a high risk of endocarditis or infection of endoprostheses. However, preventive antibiotic treatment should not be omitted.

Clinical Relevance:

Scientific Rationale for Study: Before undergoing dental treatment, patients at a high risk for endocarditis or inflammation of endoprosthesis are encouraged to take prophylactic antibiotics to kill vital bacteria that have entered the bloodstream. However, antibiotics do not hinder vial bacteria's passage into the host organism. Intensive rinsing with PVP-iodine before and during biofilm disruption might be an alternative approach to lower the risk of bacteremia.

Principal Findings: Rinsing with PVP-iodine before and during subgingival instrumentation significantly lowers the risk for post-treatment bacteremia and the number of CFU in cases of bacteremia and seems to prevent bacteremia, especially from anaerobic strains.

Practical Implications: Patients with a limited health status might benefit from the described rinsing regime.

Introduction

Periodontitis is a common inflammatory disease (Albandar & Rams 2002, Loe 1983, Oliver et al. 1998) characterized by a progressive loss of the tooth-supporting hard and soft tissues (Flemmig 1999). The primary cause for this pathologic condition is biofilms that colonize and subsequently mature on the affected root surfaces (Sanz & van Winkelhoff 2011). The bacterial composition is characterized by a high proportion of Gram-negative anaerobes (Komiya Ito et al. 2010, Socransky et al. 1998, van Winkelhoff et al. 2002). Located in direct proximity to well-perfused tissues such as gingiva and the periodontal ligament, these bacteria induce chronic inflammation by the host (Tatakis & Kumar 2005), which is triggered mainly by means of lipopolysaccharides. (Bascones et al. 2005).

Theories regarding the effects of chronically inflamed periodontal wound surfaces on general health have long been considered. Ongoing research has provided strong evidence for the bidirectional association of diabetes mellitus and periodontitis, while recent studies on periodontitis and rheumatoid arthritis or cardiovascular diseases show growing evidence of a relationship beyond just an association (de Pablo et al. 2009, Kiran et al. 2005, Tonetti & Van Dyke 2013). The linkage is generally explained by a periodic contamination of the blood stream by bacteria and their metabolites derived from subgingival wounds. Both might enter the blood circulation in elevated concentrations during daily activities such as chewing and tooth-brushing. In addition, mechanical root debridement, as the essential component of initial periodontal therapy, may cause bacteremia. While a subsequent functional impairment of the endothelium's physiological capability to regulate blood flow rate is a short effect (Tonetti et al. 2007), bacterial adherence and the proliferation of living bacteria on non-shedding surfaces of artificial endoprostheses, such as artificial joints or heart

valves, are still important subjects of ongoing discussion concerning their associated infective health risks (Zimmerli et al. 2004). Therefore, guidelines recommend the preventive systemic administration of antibiotics before dental treatment, especially for well-defined high-risk patients (Wilson et al. 2008). Despite the fact that some studies showed that the antibiotic approach might be highly potent in terms of bactericidal effects on circulating germs in the bloodstream (Denning et al. 1984), this medication does not actually provide a safe elimination of bacteria (Seo et al. 2014, Duvall et al. 2013)} or any obstacle for the transition of viable bacteria into the bloodstream.

PVP-iodine is a cheap broad-spectrum antiseptic agent frequently used in the therapy of periodontitis, especially in Scandinavia (Rosling et al. 2001) and Switzerland (Sahrmann et al. 2014). Its spectrum of action covers bacteria associated with periodontitis (Reimer et al. 1998) and its use as a rinse during initial periodontal therapy has been proven to provide a significant therapeutic benefit in terms of pocket depth reduction (Sahrmann et al. 2014). Nevertheless, there is only weak data regarding its effect on the prevention of oral-borne bacteremia during initial periodontitis therapy. Discordant results regarding bacteremia have been obtained from studies that performed instrumentation with ultrasonic devices or with hand instruments (Cherry et al. 2007, Witzenberger et al. 1982). Notably, none of these studies applied the antiseptic during subgingival instrumentation, when the disruption of the biofilms actually occurs.

Therefore, it was the aim of the present study to assess the impact of PVP-iodine rinsing before ultrasonic root instrumentation and concomitantly with this instrumentation on the prevalence and the extent of oral-borne bacteremia in patients with chronic periodontitis.

Materials & Methods

Study design

The present study was conducted as a single-center, randomized, placebo-controlled clinical study with a split-mouth cross-over design. The study protocol was approved by the liable Ethical Committee of Zurich, Switzerland (KEK-Zh-Nr. 2011-0076) and authorized by the responsible national authority for the observation of therapeutic products (Swissmedic, Berne, Switzerland, registration number 2012DR3047). The study was notified in the registry database of the U.S. National Institutes of Health (www.Clinicaltrials.com, identifier NCT01647347) and was conducted in accordance with

the guidelines of Good Clinical Practice and the revised Declaration of Helsinki for clinical studies (Morris 2013). The entire study process was monitored by an external facility (Clinical Trials Center, Zurich, Switzerland). As previously planned, clinical and office performance was scrutinized during five monitoring sessions during the entire study process.

Study population

While feasible data for a reasonable power analysis were missing, it was planned to conduct the study on 20 patients.

The study was composed of male and female patients over 18 years of age with moderate or severe chronic periodontitis with at least 2 sites with PD ≥ 5 mm in each quadrant. Patients with systemic diseases or medications known to interfere with periodontal therapy were not included. Furthermore, patients who underwent antibiotic therapy or anticoagulation therapy during the preceding 6 months, those on thyroid medication or with a known allergy to PVP-iodine were excluded from this study. Females who were pregnant or breastfeeding were also not included in this trial.

Outpatients visiting the Clinic of Preventive Dentistry, Cariology and Periodontology of the University of Zurich for periodontal treatment were screened for possible inclusion (PhS).

Clinical procedure

A computer-randomized list was generated (AM) prior to the start of the study. Accordingly, groups indicating the treatment modalities (i.e., test or control treatment) and the treatment allocation (i.e., left or right half of the mouth) for the first appointment were prepared and placed into non-transparent envelopes. The envelopes were numbered from 1 to 20, according to the chronological order of the consecutively enrolled patients. The contents were concealed until immediately before the first treatment.

After the first visit with the presentation of the study and the delivery of written patient information and the consent form, all questions regarding the study were addressed in a second meeting before patient agreement was finally received.

Study treatment was performed as follows (see Figure 1):

During the first appointment, the envelope with the group was opened and the allocation of the first course of instrumentation, i.e., left or right half of the mouth, and the solution to be applied was defined: PVP-iodine for the test or tap water for the control treatment.

After local anesthesia was administered to areas with deep periodontal sites of the appropriate half of the oral cavity, the patient rinsed the mouth for exactly one minute with the corresponding test or

control liquid. Meanwhile, a tourniquet was loosely placed around the upper arm, and the bend of the elbow was disinfected twice with Kodan® (Schülke & Mayr AG, Zurich, Switzerland). Then, all periodontal sites in the area of interest were rinsed for another 60 sec with the same liquid using a 10 ml single-use plastic syringe and a blunt tip with an inner diameter of 0.49 mm (Endo-EZE tip, Ultradent, UT South Jordan). Thereafter, these pockets were instrumented using an ultrasonic-driven device (CavitronPlus® and Slimline inserts, Dentsply deTrey, Graz, Austria) at the highest settings for power and lavage to churn up a maximum of subgingival biofilm for 60 seconds. During the study process, the ultrasonic device ran with the according liquids provided from the external cooling tank. Exactly 3 minutes after the start of the subgingival instrumentation, a blood sample of 10 ml was taken from the most visible arm vein after tightening the tourniquet. For the sampling, a combination of a Vacuette Viso Plus needle (Greiner Bio-One GmbH, Kremsmünster, Austria) and a vacuum isolator tube (Isolator 10, Oxoid AG, Pratteln, Switzerland) was used. Immediately after the sampling, the extraction site was compressed for at least 2 min. Finally, the sampling site was covered by an adhesive plaster.

The second treatment was performed after a wash-out period of at least two weeks. The treatment was performed in line with the first treatment. However, in this case, the not yet allocated liquid was used in the remaining half of the mouth.

Samples were labeled and stored in a dark place at room temperature until they were processed in the laboratory.

Beyond the study protocol, proper periodontal therapy was provided in the according quadrants after performing the study at the same appointments.

Microbiological analysis

According to the study protocol, all samples were required to be processed within 8 hours after extraction. Due to the coding of the glass tubes, the microbiology staff was blinded regarding the treatment type of the corresponding blood samples.

First, the samples were centrifuged at 3500 g for 10 min (Thermo Fisher Scientific, Heraeus LABOFUGE 400 Centrifuge, Hanau, Germany). Care was taken to allow an undisturbed coasting to standstill in order to not re-disperse the centrifugate. Following a standardized method, the supernatant was removed with a pipette (Oxoid AG, Pratteln, Switzerland). After vortexing the remnants, three drops (app. 150 µl) were applied in each of the following culture media and dispensed with a wire loop: Columbia Agar + 5% sheep blood (COS, BioMérieux, Genève, Switzerland), Brucella agar (Becton Dickinson, Allschwil, Switzerland), Chocolat PolyViteX agar (PVX, BioMérieux), Mac Conkey agar (MCK, BioMérieux), Columbia CNA agar + 5% sheep blood (CNA, BioMérieux). The remaining material was placed into thioglycolate growing medium (Becton Dickinson).

The growing media were cultured under aerobic (MCK) and anaerobic (all others) conditions at 37°C for 2-3 d. As soon as colonies were visible, they were counted and subcultured. Identification was performed according to the standard procedures using partially commercial biochemical test kits and Matrix-Assisted Laser Desorption Ionization Time-of-Flight Mass Spectrometry (X2 Bruker MALDI-TOF Biotyper, Bruker Daltonik GmbH, Bremen, Germany).

Determination of the inflamed area

Based on a standardized methodology (Hujoel et al. 2001)(Nesse et al. 2008), the overall (PESA) and inflamed periodontal surface area (PISA) for each individual patient and the instrumented periodontal sites per group were calculated. For this purpose, the clinical parameters of periodontal pocket depths (PD) and attachment loss (AL) were used. In short, clinical data from the periodontal findings sheet were transferred and inserted into an Excel spreadsheet to automatically calculate the total epithelialized and inflamed surfaces from the pocket depth, recession and BOP data, based on reference data for the anatomy of the individual teeth.

Statistical analysis

Data were entered into a web-based electronic data-capture program (secuTrial®, interActive Systems GmbH, Berlin, Germany) by the first author and controlled for entry errors by an external monitor. Statistical tests were performed using SPSS 22 for Macintosh (IBM, New York, USA). Data were tested for normal distribution (Kolmogorov-Smirnov goodness-of-fit test). To test for differences between discrete values, i.e., the prevalence of bacteremia between the groups, the McNemar test was performed. Intergroup differences for the number of bacteremia events and the number of colony forming units (CFU) per case of bacteremia were tested for differences using the non-parametric Wilcoxon test in cases of skewed data distribution. Logistic regression analysis was performed using the Spearman coefficient for two continuous variables and Fisher's exact test to assess the significance of the association between the patient's or clinical parameters (PD, BOP, PESA or PISA, gender) and the bacteremia parameters. Furthermore, statistical tests to assess a possible effect of sources of variability generally linked to crossover experiments were performed (pkcross, Stata® vs. 13, StataCorp LP, College Drive, Texas, USA). The level of significance for all tests was set at 5 % ($p \leq 0.05$).

Results

Twenty patients were enrolled in the study. As the second blood sample of patient No. 7 was destroyed during centrifugation, a microbiologic analysis could not be performed. Therefore, the data from only 19 patients were used.

Baseline clinical data (PI, BOP, number of sites with deep probing depths, mean probing depth, mean PESA or PISA) for both groups are listed in Table 1. The Wilcoxon test did not reveal any statistically significant differences between the groups.

Table 2 displays the number and species of culturable bacteria in each group. In summary, bacteria of oral origin included different *Streptococcus* spp., *Lactobacillus* spp. and facultative anaerobic bacteria such as *Actinomyces* spp. but also strictly anaerobic bacteria such as *Prevotella* spp, *Clostridium* spp. and *Fusobacterium* spp.

Bacteremia was found in 11/19 cases in the control group and in 5/19 cases in the test group. After the exclusion of cases with typical skin bacteria species, 10/19 (53%) oral-borne bacteremia were found in the control group and 2/19 (11%) in the test group. The McNemar test revealed a significantly reduced risk for the prevalence of bacteremia of oral origin ($p = 0.0133$) when PVP-iodine was used. When the average number of colony forming units per case of oral-borne bacteremia was calculated, 12.2 [1;46] in the control and 3.0 [1;5] in the test group were found. The Wilcoxon test showed a significantly smaller number of oral-borne bacteria per case of bacteremia for the test group compared to the control group ($p = 0.003$). Comparing the ratio of aerobic and anaerobic bacteria in the two groups, 83.0% turned out to be anaerobic species in the control group, whereas there was no anaerobic colony found within the test group (Fig. 2). No patients reported adverse effects after the use of PVP-iodine.

Multiple regression revealed no correlation of the parameters BOP, PI, number of sites ≥ 4 mm, PESA or PISA with the prevalence of bacteremia (p-values 0.087, 0.245, 0.214, 0.242, 0.417) or with the number of bacteria per case of bacteremia (p-values 0.868, 0.310, 0.493, 0.802 and 0.672, respectively). However, there was a correlation of BOP and the number of sites > 4 mm ($p = 0.004$).

Discussion

In the present study, we assessed the effect of an intensive rinsing regimen with 10% PVP iodine on post-treatment bacteremia after subgingival ultrasonic instrumentation of root surfaces in patients with chronic periodontitis. To the best of the authors' knowledge, this study is the first to assess the antiseptic's effect during subgingival biofilm disruption. After one minute of mouth washing, one minute of subgingival rinsing and one minute of subgingival instrumentation of all periodontal pockets during PVP-iodine application, we found significantly less bacteria of oral origin in blood samples that were taken from the central blood flow three minutes after periodontal instrumentation had begun, compared to the same treatment with tap water. A significantly lower incidence of bacteremia was

found in the test group, and bacteremia was less pronounced in terms of the number of viable counts in the blood samples.

Bacteremia is a frequent finding after dental treatment (Parahitiyawa et al. 2009). After subgingival scaling during non-surgical periodontal therapy, post-treatment bacteremia of oral origin occurs in 55-70% of cases (Waghmare et al. 2013, Witzenberger et al. 1982), with a 72-78% involvement of anaerobes (Brook 2010). Data from the present control group showed a comparable incidence of 60% and a contribution of 82% of anaerobic species. A study from the early 1980s failed to show any effect of subgingival rinsing with PVP-iodine (Witzenberger et al. 1982) in patients with an average pocket depth of only 3.3 mm. In contrast to the present study, in those studies, no antiseptic was applied during instrumentation, i.e., during the mechanical disruption of the biofilms. Furthermore, in the cited studies, the microbiological analysis failed to distinguish between bacteremia of oral origin and that from the skin or external contamination. In the present study, however, in 25% of the samples, bacterial species were found that could not be assigned to the oral flora, despite the fact that sampling and processing of the blood were performed under strict clinical and laboratory quality standards. Likewise, in a recent study on the use of 7.5% PVP iodine to prevent bacteremia after mechanical gingivitis treatment, contamination by non-oral germs was found in 40% of the cases (Cherry et al. 2007). It is important to mention that in the latter study, no antiseptic was applied during instrumentation. However, the risk for bacteremia was also significantly lowered by an odds ratio of 0.189 and was reported to be approximately 80% more effective (Cherry et al. 2007). In that study, periodontal pockets accounted for mean probing depths of 2.2 ± 0.4 mm, which was considerably less than in the present study, with mean probing pocket depths of 6.0 mm in both groups. Therefore, a higher rate of bacteremia might be expected. However, even subgingival rinsing with water or saline alone, as in our control group, reduces the risk of bacteremia, as was previously shown (Witzenberger et al. 1982, Rahn 1993). On the other hand, via the use of a special lysis system in the present study that allowed for disruption of eukaryote cells and therefore detection of intracellular bacteria, a more exact analysis of bacterial species could be performed. Therefore, an incidence of bacteremia of 60 % in our control group seemed reasonable.

The present study was performed using a cross-over split mouth design. Though inter-individual variability might be decreased, it is not impossible that the sequence of control and test treatments might have affected the outcome. Apart from the fact that both treatment sequences (test – control or control – test) were performed in equal ratios, we performed a statistical analysis to assess the possible effect of the sequence or period as sources of variability generally linked to cross-over experiments (pkcross, Stata® Vs. 13, StataCorp LP, College Drive, Texas, USA). No indication of an

effect of sequence or period was found, and no indication for the presence of a carry-over effect was found.

The wound area in both groups was comparable. We aimed to include the assessment of this aspect to foreclose any differences in the originally lacerated wound area, which might have affected the outcomes. Several attempts have been performed so far to assess the overall size of the inflamed area. Assuming a mean periodontal breakdown of one-third of the root length, Jepsen and co-workers estimated a total of 20 cm^2 of chronically inflamed tissue area (Jepsen 1963). Other studies suggested considerably larger wound areas of between 70 and 90 cm^2 (Loos 2006). To estimate and characterize the total wound size as appropriately as possible, Hujoel et al. used a more sophisticated approach to determine the overall area. Therefore, the cone shape of the root surfaces and different root anatomies and consequently the enhanced wound area for the initial attachment loss were taken into consideration (Hujoel et al. 2001). Based on their publication, evaluation tables were published for the calculation of the overall epithelialized (PESA) or inflamed periodontal surface area (PISA) for individual patients, which were applied using the documented periodontal pocket depths and attachment losses of our patients (Nesse et al. 2008).

Within this study, one single blood sample was taken 3 min after each treatment. Several studies collected a blood sample before treatment to ensure a bacteremia-free baseline status. Although such an approach might be ideal an ideal pre-condition, it still presents some disadvantages. Therefore, we changed this approach, mainly for the following two reasons: First, previous studies with 20 and 60 patients, respectively, showed the complete absence of oral bacteria in all samples before treatment (Cherry et al. 2007, Witzenberger et al. 1982), and subgingival water rinsing did not seem to provoke bacteremia (Witzenberger et al. 1982). Second, there is a practical disadvantage of additional baseline sampling: either a second puncture of the vein and accordingly more discomfort for the patient, or an in-dwelling cannula would have to be placed during several time points. The latter, however, allows for bacterial colonization of the device between the samplings and therefore distorts the results.

The time point for sampling was set in accordance with studies investigating the bacterial profile in the central blood stream after other dental interventions such as tooth brushing, tooth extraction, pulp manipulation and professional cleaning (Brennan et al. 2007, Lockhart et al. 2007). These studies showed that the number of viable bacteria in the blood reached their maximum between the 2nd and the 3rd post-interventional minutes before declining again during the consecutive hour.

As an antiseptic agent, PVP-iodine at a concentration of 10% was chosen, as it has been recommended as a first-choice solution to reduce oral pathogens by mouth wash or rinsing due to a quicker and more pronounced bactericidal effect compared to 0.2% chlorhexidine, the most popular antiseptic agent in dentistry (Rahn 1993, Rahn et al. 1995).

Despite our pursuit of a sophisticated study design, there are still shortcomings of our study. The study was conducted as a split-mouth study, which bears the intrinsic risk of the test treatment confounding the results of the control site and *vice versa*. However, choosing this methodological approach, we could benefit from advantages such as more adequately equilibrated environmental factors including smoking, general health and stress. In fact, our baseline data showed no significant differences. With a wash–out period of at least 2 weeks, an ample time span was set to avoid reciprocal treatment effects as much as possible. Furthermore, according to the study protocol, no proper cleaning of the pocket areas could be performed, but we aimed for a quick instrumentation to disrupt as much biofilm as quickly as possible. Therefore, a sharp rise in the prevalence and severity of bacteremia was evoked. In doing so, blood sampling could be performed at well-defined time points at the previously discussed maximum peak of bacteremia. However, proper scaling and root planing were performed after blood sampling and not as part of the study treatment.

By culturing bacteria from the blood samples, only viable bacteria were screened. Therefore, we could not identify bacterial components and bacteria that were already eliminated by the immune system of the healthy subjects, bacteria that transformed into a non-cultivable state despite remaining vital, or bacteria that did not survive until being processed. In addition, the analysis is highly technique-sensitive, as some bacteria might not survive the culturing process or at least would not form colonies (Wardle 1997). With highly specific tests based on genetic analysis methods (FISH etc.), it would have been possible to expand the search for selected bacteria. However, as there were no specific strains or bacteria of interest, we refrained from doing so in the present study.

The detected bacteria represent a variety of species. The spectrum included anaerobic Gram-negative and –positive rods, anaerobic Gram-positive cocci, as well as typical periodontal marker bacteria such as *Fusobacterium* spp.*, Porphyromonas gingivalis*, *Fusobacterium nucleatum* and *Prevotella intermedia.* Accordingly, the spectrum covers a wide range of different germs and is in accordance with the findings of other studies (Cherry et al. 2007, Forner et al. 2006, Lockhart et al. 2008, Witzenberger et al. 1982), specifically *Streptococci viridans* and *Aggregatibacter* spp., which are frequently involved in endocarditis lesions or are associated with inflammation of prosthetic heart valves, shunts or catheters (Zimmerli et al. 2004).

In the context of the present study, however, it is important to state that transient bacteremia might occur several times a day, caused by tooth brushing or even chewing (Forner et al. 2006, Lockhart et al. 2008). In healthy patients, their acute impact on health is negligible. However, it

was shown that bacteremia is followed by an inflammation of the endothelium, which results in hampered endothelial function 24 h after periodontal treatment in healthy patients (Tonetti 2009). High-risk patients, as defined by the American Heart Association (Wilson et al. 2008), or patients in intensive care (such as mechanically ventilated patients) face a strongly enhanced risk of developing infections caused by the proliferation of oral-borne bacteria (Jones et al. 2010). These complications, namely endocarditis and infections of endoprostheses, stand out due to significant treatment costs and high morbidity due to invasive surgery and mortality (Fink et al. 2008). According to the guidelines, these patients are encouraged to take broad-spectrum antibiotics one hour before each dental consultation to avoid the circulation of bacteria that may be displaced by any action that leads to a bleeding in the oral cavity. Against the background of growing antimicrobial resistance of anaerobic bacteria (Brook 2010), these patients might benefit from any effective measure to additionally lower the bacterial load in the central blood stream and accordingly should be pretreated before and during instrumentation with a rinse of 10% PVP-iodine.

Conclusion

Rinsing with 10% PVP-iodine significantly reduces the risk for post-treatment bacteremia during non-surgical periodontal therapy. Rinsing therefore seems to be recommendable, especially in patients with a high risk for endocarditis or infection of endo-prostheses. As the incidence of bacteremia seems to not be completely eliminable, however, preventive antibiotic treatment should not be omitted in high-risk patients.

References

Albandar, J. M. Rams, T. E. (2002) Risk factors for periodontitis in children and young persons. Periodontol 2000 **29,** 207-222.

Bascones, A.Noronha, S.Gomez, M.Mota, P.Gonzalez Moles, M. A. Villarroel Dorrego, M. (2005) Tissue destruction in periodontitis: bacteria or cytokines fault? Quintessence Int **36,** 299-306.

Brennan, M. T.Kent, M. L.Fox, P. C.Norton, H. J. Lockhart, P. B. (2007) The impact of oral disease and nonsurgical treatment on bacteremia in children. J Am Dent Assoc **138,** 80-85.

Brook, I. (2010) The role of anaerobic bacteria in bacteremia. Anaerobe **16,** 183-189.

Cherry, M.Daly, C. G.Mitchell, D. Highfield, J. (2007) Effect of rinsing with povidone-iodine on bacteraemia due to scaling: a randomized-controlled trial. J Clin Periodontol **34,** 148-155.

de Pablo, P.Chapple, I. L.Buckley, C. D. Dietrich, T. (2009) Periodontitis in systemic rheumatic diseases. Nat Rev Rheumatol **5,** 218-224.

Denning, D. W.Cassidy, M.Dougall, A. Hillis, W. S. (1984) Failure of single dose amoxycillin as prophylaxis against endocarditis. Br Med J (Clin Res Ed) **289,** 1499-1500.

Duvall, N. B.Fisher, T. D.Hensley, D.Hancock, R. H. Vandewalle, K. S. (2013) The comparative efficacy of 0.12% chlorhexidine and amoxicillin to reduce the incidence and magnitude of bacteremia during third molar extractions: a prospective, blind, randomized clinical trial. Oral Surg Oral Med Oral Pathol Oral Radiol **115,** 752-763.

Fink, B.Makowiak, C.Fuerst, M.Berger, I.Schafer, P. Frommelt, L. (2008) The value of synovial biopsy, joint aspiration and C-reactive protein in the diagnosis of late peri-prosthetic infection of total knee replacements. J Bone Joint Surg Br **90,** 874-878.

Flemmig, T. F. (1999) Periodontitis. Ann Periodontol **4,** 32-38.

Forner, L.Larsen, T.Kilian, M. Holmstrup, P. (2006) Incidence of bacteremia after chewing, tooth brushing and scaling in individuals with periodontal inflammation. J Clin Periodontol **33,** 401-407.

Hujoel, P. P.White, B. A.Garcia, R. I. Listgarten, M. A. (2001) The dentogingival epithelial surface area revisited. J Periodontal Res **36,** 48-55.

Jepsen, A. (1963) Root surface measurement and a method for x-ray determination of root surface area. Acta Odontol Scand **21,** 35-46.

Jones, D. J.Munro, C. L.Grap, M. J.Kitten, T. Edmond, M. (2010) Oral care and bacteremia risk in mechanically ventilated adults. Heart Lung **39,** S57-65.

Kiran, M.Arpak, N.Unsal, E. Erdogan, M. F. (2005) The effect of improved periodontal health on metabolic control in type 2 diabetes mellitus. J Clin Periodontol **32,** 266-272.

Komiya Ito, A.Ishihara, K.Tomita, S.Kato, T. Yamada, S. (2010) Investigation of subgingival profile of periodontopathic bacteria using polymerase chain reaction. Bull Tokyo Dent Coll **51,** 139-144.

Lockhart, P. B.Brennan, M. T.Sasser, H. C.Fox, P. C.Paster, B. J. Bahrani-Mougeot, F. K. (2008) Bacteremia associated with toothbrushing and dental extraction. Circulation **117,** 3118-3125.

Lockhart, P. B.Loven, B.Brennan, M. T. Fox, P. C. (2007) The evidence base for the efficacy of antibiotic prophylaxis in dental practice. J Am Dent Assoc **138,** 458-74; quiz 534-5, 437.

Loe, H. (1983) Principles of aetiology and pathogenesis governing the treatment of periodontal disease. Int Dent J **33,** 119-126.

Loos, B. G. (2006) Systemic effects of periodontitis. Ann R Australas Coll Dent Surg **18,** 27-29.

Morris, K. (2013) Revising the Declaration of Helsinki. Lancet **381,** 1889-1890.

Nesse, W.Abbas, F.van der Ploeg, I.Spijkervet, F. K.Dijkstra, P. U. Vissink, A. (2008) Periodontal inflamed surface area: quantifying inflammatory burden. J Clin Periodontol **35,** 668-673.

Oliver, R. C.Brown, L. J. Loe, H. (1998) Periodontal diseases in the United States population. J Periodontol **69,** 269-278.

Parahitiyawa, N. B.Jin, L. J.Leung, W. K.Yam, W. C. Samaranayake, L. P. (2009) Microbiology of odontogenic bacteremia: beyond endocarditis. Clin Microbiol Rev **22,** 46-64, Table of Contents.

Rahn, R. (1993) Review presentation on povidone-iodine antisepsis in the oral cavity. Postgrad Med J **69 Suppl 3,** S4-9.

Rahn, R.Schneider, S.Diehl, O.Schafer, V. Shah, P. M. (1995) Preventing post-treatment bacteremia: comparing topical povidone-iodine and chlorhexidine. J Am Dent Assoc **126,** 1145-1149.

Reimer, K.Schreier, H.Erdos, G.Konig, B.Konig, W. Fleischer, W. (1998) [Molecular effects of a microbicidal substance on relevant microorganisms: electron microscopic and biochemical studies on povidone-iodine]. Zentralbl Hyg Umweltmed **200,** 423-434.

Rosling, B.Hellstrom, M. K.Ramberg, P.Socransky, S. S. Lindhe, J. (2001) The use of PVP-iodine as an adjunct to non-surgical treatment of chronic periodontitis. J Clin Periodontol **28,** 1023-1031.

Sahrmann, P.Imfeld, T.Ronay, V.Attin, T. Schmidlin, P. R. (2014) Povidone-iodine gel and solution as adjunct to ultrasonic debridement in nonsurgical periodontitis treatment: an RCT pilot study. Quintessence Int **45,** 281-290.

Sanz, M. van Winkelhoff, A. J. (2011) Periodontal infections: understanding the complexity--consensus of the Seventh European Workshop on Periodontology. J Clin Periodontol **38 Suppl 11,** 3-6.

Seo, S. K.Xiao, K.Huang, Y. T.Jongwutiwes, U.Chung, D.Maloy, M.Giralt, S.Barker, J. N.Jakubowski, A. A. Papanicolaou, G. A. (2014) Impact of peri-transplant vancomycin and fluoroquinolone administration on rates of bacteremia in allogeneic hematopoietic stem cell transplant (HSCT) recipients: a 12-year single institution study. J Infect **69,** 341-351.

Socransky, S. S.Haffajee, A. D.Cugini, M. A.Smith, C. Kent, R. L. J. (1998) Microbial complexes in subgingival plaque. J Clin Periodontol **25,** 134-144.

Tatakis, D. N. Kumar, P. S. (2005) Etiology and pathogenesis of periodontal diseases. Dent Clin North Am **49,** 491-516, v.

Tonetti, M. S. (2009) Periodontitis and risk for atherosclerosis: an update on intervention trials. J Clin Periodontol **36 Suppl 10,** 15-19.

Tonetti, M. S.D'Aiuto, F.Nibali, L.Donald, A.Storry, C.Parkar, M.Suvan, J.Hingorani, A. D.Vallance, P. Deanfield, J. (2007) Treatment of periodontitis and endothelial function. N Engl J Med **356,** 911-920.

Tonetti, M. S. Van Dyke, T. E. (2013) Periodontitis and atherosclerotic cardiovascular disease: consensus report of the Joint EFP/AAP Workshop on Periodontitis and Systemic Diseases. J Clin Periodontol **40 Suppl 14,** S24-9.

van Winkelhoff, A. J.Loos, B. G.van der Reijden, W. A. van der Velden, U. (2002) Porphyromonas gingivalis, Bacteroides forsythus and other putative periodontal pathogens in subjects with and without periodontal destruction. J Clin Periodontol **29,** 1023-1028.

Waghmare, A. S.Vhanmane, P. B.Savitha, B.Chawla, R. L. Bagde, H. S. (2013) Bacteremia following scaling and root planing: A clinico-microbiological study. J Indian Soc Periodontol **17,** 725-730.

Wardle, H. M. (1997) The challenge of growing oral spirochaetes. J Med Microbiol **46,** 104-116.

Wilson, W.Taubert, K. A.Gewitz, M.Lockhart, P. B.Baddour, L. M.Levison, M.Bolger, A.Cabell, C. H.Takahashi, M.Baltimore, R. S.Newburger, J. W.Strom, B. L.Tani, L. Y.Gerber, M.Bonow, R. O.Pallasch, T.Shulman, S. T.Rowley, A. H.Burns, J. C.Ferrieri, P.Gardner, T.Goff, D. Durack, D. T. (2008) Prevention of infective endocarditis: guidelines from the American Heart Association: a guideline from the American Heart Association Rheumatic Fever, Endocarditis and Kawasaki Disease Committee, Council on Cardiovascular Disease in the Young, and the Council on Clinical Cardiology, Council on Cardiovascular Surgery and Anesthesia, and the Quality of Care and Outcomes Research Interdisciplinary Working Group. J Am Dent Assoc **139 Suppl,** 3S-24S.

Witzenberger, T.O'Leary, T. J. Gillette, W. B. (1982) Effect of a local germicide on the occurrence of bacteremia during subgingival scaling. J Periodontol **53,** 172-179.

Zimmerli, W.Trampuz, A. Ochsner, P. E. (2004) Prosthetic-joint infections. N Engl J Med **351,** 1645-1654.

Figure 1

Flow-chart of the study protocol

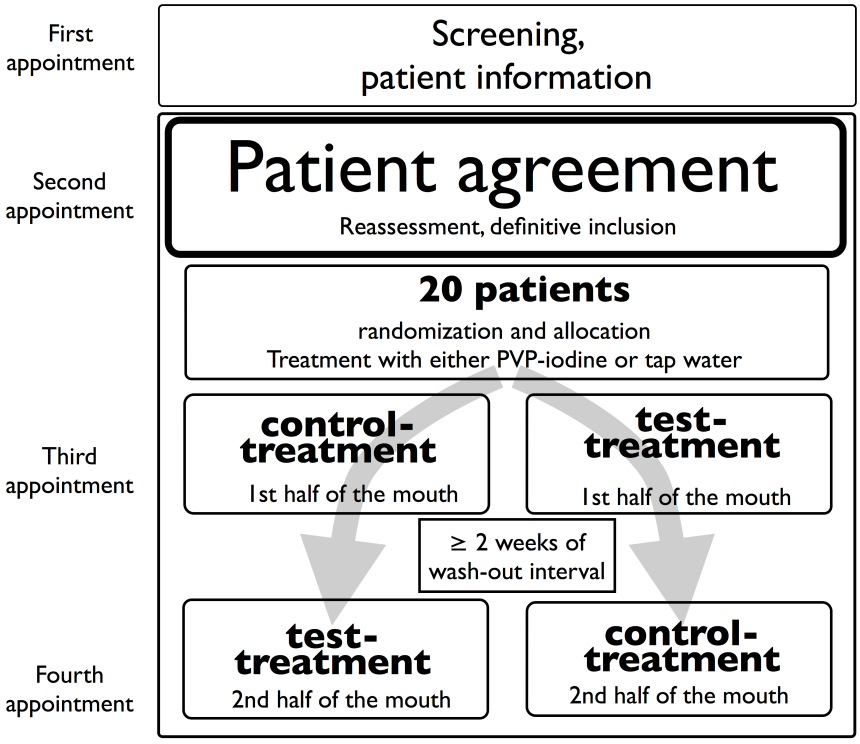
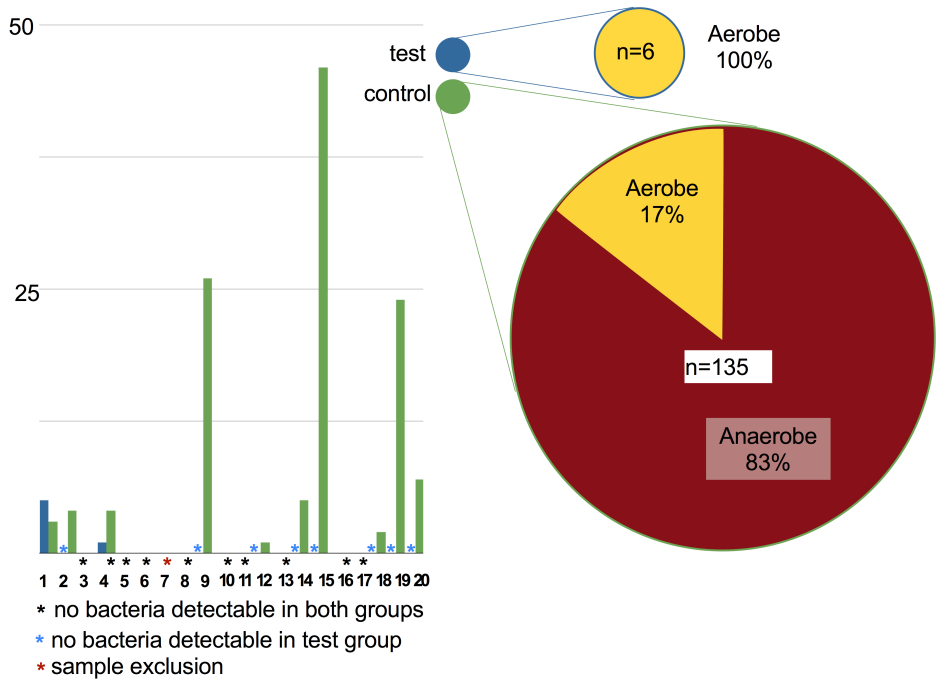


Figure 2

Incidence of bacteremia and proportion of aerobe and anaerobe colonies per group.



Tables

Table 1

Baseline data for both groups (means ± standard deviations)

	Control	**Test**	**P**
Age [y]	52.7±11.9		
Gender [m/f]	80/20		
PI [%]	58.7±31.1	53.4±31.4	0.884
BOP [%]	54.0±25.3	51.4±26.8	0.794
PPD > 4 mm [n]	19.8±13.9	20.7±13.3	0.841
Mean PPD [mm]	6.0±0.8	6.0±1.7	0.897
PESA [mm^2]	917.8±422.9	1009.4±485	0.562
PISA [mm^2]	504.0±375.9	665.5±474.1	0.279

Table 2

Presentation of the individually identified bacteria and the counts of viable bacteria in the respective blood samples (in brackets).

Patient number	**Control (water)**		**Test (PVP-iodine)**	
	Non-oral	Oral	Non-oral	Oral
1		*Parvimonas micra* (3)	*Proprionibacterium acnes* (2) *Staphylococcus hominis* (1)	*R. dentocariosa* (2) Streptococcus viridans (3)
2	*S. hominis (*2)	*P. micra* (1) Streptococcus viridans (3)	*P. acnes* (1)	-
3	-	-	-	-
4	-	*P. micra* (2) *Streptococcus constellatus* (2)	-	*Streptococcus mitis/oralis* (1)
5	-	-	-	-
6	-	-	-	-
7 (excluded)	*(Sample damaged)*	*(Sample damaged)*	-	-
8	-	-	-	-
9	*Dermatobacter hominis* (1)	*Veillonella* spp. (1) *P. micra* (4) *Prevotella intermedia* (4) *S. constellatus* (2) *Atopobium rimae* (2) - Anaerobe Gram-rods (8) - Anaerobe Gram+ rods (4) - Anaerobe Gram+ coccus (1)	-	-
10	-	-	-	-
11	-	-	-	-
12	-	*Streptococcus anginosus* (1)	-	-
13	-	-	-	-
14	*P. acnes* (2)	*P. micra* (1) *Fusobacterium* spp. *(4)*	*P. acnes* (1) *Corynebacterium accolens* (2)	-

15	-	*S. anginosus* (11) *Aggregatiabacter aphrophilus* (6) *Fusobacterium* spp. (8) *P. micra* (8) - Anaerobe Gram+ rods (3) - Anaerobe Gram+ cocci (6) - Anaerobe Gram- rods (4)	-	-
16	-	-	-	-
17	*P. acnes* (2) *S. hominis* (2)	-	-	-
18	*P. acnes* (1) *Propriobacterium avidum* (1)	*S. mitis* (2)	*P. acnes* (1)	-
19	-	Anaerobe Gram- rods (4) *Actinomyces spp.* (14) *A. meyeri* (4) *P. intermedia* (2)	-	-
20	-	*Clostridium* spp. (4) *Fusobacterium nucleatum* (1) *Porphyromonas gingivalis* (1) *Lactobacillus* spp. (1)	-	-